REMARKS/ARGUMENTS

Upon entry of this amendment, claims 1-6, 9-14, 128, and 137, are pending in the instant application. Claims 1 and 128 have been amended. Claims 7 and 8 have been cancelled, and Applicants reserve the right to prosecute that subject matter, as well as the originally presented claims, in continuing applications.

I. Oath/Declaration

The Examiner has indicated that Applicants have not provided an appropriate response to the objection to the Oath/Declaration set forth in the prior Office Action (9/23/03). The Examiner has asserted that the Declaration is defective because a "non-initialed and/or non-dated alterations have been made to the oath or declaration." Applicants have obtained a Supplemental Declaration executed by Kristin Marshall and Eric Davidson (2 counterparts), in compliance with 37 C.F.R. § 1.67(a), and submit it with the instant response.

II. Claim Rejections Under 35 U.S.C. § 112, first paragraph

Claims 1-14, 128, and 137 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Examiner notes that the specification provides only one example of a polynucleotide that is regulated by a peptide effector, the Rev dependent RNA ligase ribozyme, found in Example 4. Examiner goes on to argue "the specification as filed provides insufficient written description to support the genus of polynucleotides and peptide effectors, encompassed by the instantly claimed invention". However, the specification as filed describes more than one species within a genus. Applicants have provided several examples of polynucleotides that are regulated by a peptide effector in addition to the Rev dependent RNA ligase ribozyme. Specifically, Example 3 (see page 45) provides a detailed description of the *in vitro* selection and identification of two other examples of polypeptide dependent regulatable, catalytically active nucleic acids (hereinafter "RCANA"), the Cyt18 dependent ribozyme ligase, and the hen egg white lysozyme dependent ribozyme ligase. Although the Cyt18 and lysozyme dependent constructs are sometimes referred to as

protein-dependent RCANAs, Applicants have defined the terms "protein", "polypeptide", and "peptide" in the specification (page 32, paragraph 101) as compounds comprising amino acids joined via peptide bonds, and the terms are used throughout the specification interchangeably. In addition, Example 3 and Example 4 provide data describing physical and chemical properties of the peptide dependent RCANAs identified, *e.g.*, ligand specificity, and catalytic activity.

Examiner also cites MPEP § 2163, which states "A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." Applicants indicate the sequences and structures for several protein-dependent, regulatable, catalytically active nucleic acid sequences. Figure 19(a) shows the nucleic acid sequences for six Cyt18 dependent ribozyme ligase clones, and four lysozyme dependent ribozyme ligase clones, and Figure 19(b) shows the predicted secondary structure of a dominant Cyt18-dependent clone. Additionally, one skilled in the art would be able to recognize the catalytic domain of the polynucleotide sequence and its related structure, and would be able to distinguish the catalytic domain from the sequence and structure of regulatory domain of the polynucleotide sequence, and furthermore would be able to understand the correlation between the sequence and structure of these distinct domains, and the function they each serve. Moreover, the correlation between the structure and function is expressly stated in Claim 1, "the catalytic activity of the catalytic domain is regulated by the interaction of the peptide effector with the regulatory domain".

Examiner further argues the "Applicants have not demonstrated, apart from further experimentation, how to use the specific example set forth in the specification as filed to predict the structures of other regulated polynucleotides and their corresponding peptide effectors" (Office Action, page 3). Examiner also argues the species specifically disclosed are not representative of the genus because the genus is highly variant. Applicants traverse. Such arguments would preclude any broad genus claims in any case from being issued.

However, antibody claims to a broad genus have been allowed, *e.g.*, based on a written description that describes a method for generating and identifying such antibodies, and a few representative examples of species within the genus being claimed. Furthermore, Examiner concedes that the instant invention is enabled, and rejects only on the basis of the written

description requirement contained. Applicants note the core of the instant invention is not so much the sequences and structures of the peptide-dependent RCANAs themselves, but rather the existence of a method for generating and identifying peptide-dependent RCANAs, regardless of the sequence or secondary structure, and regardless of how many variant species exist within the genus.

Thus, the detailed description of the method for identifying peptide-dependent RCANAs, combined with the actual reduction to practice of three distinct peptide dependent RCANAs, including disclosure of clone sequences, a drawing of the predicted secondary structure, physical and chemical properties, and functional data, all clearly indicate the Applicant is in possession of the claimed invention. The Applicants respectfully request that the Examiner withdraw this rejection.

III. Claim Rejections Under 35 U.S.C. § 102

Claims 1-2, 5, 7-10, 12-13, 137 remain rejected under 35 U.S.C. 102(b) as being anticipated by George *et al.* (US Patent No. 5,834,186). The Examiner indicates George *et al.* disclose catalytic RNA polynucleotides comprising a ribozyme sequence that is linked to a ligand binding sequence, placing the activity of the ribozyme under the control of that ligand and requiring the presence of the ligand for activation or inactivation. As indicated above, claims 7 and 8 have been cancelled. Thus, the pending claims in the instant application as amended herein, expressly recites regulatable catalytically active DNA polynucleotides, not RNA. DNA polynucleotides lack ribose 2'-hydroxyl groups (contained in RNA) and are structurally different than RNA polynucleotides. The Examiner notes that George *et al.* disclose that DNA molecules with ligand binding behavior have been isolated by Ellington and Szotak, and Bock et al. However, George *et al.* do not teach regulatable, catalytically active DNA molecules such that one skilled in the art would be able to practice such an invention, it is merely prophetic. Thus, George et al. cannot anticipate the instant claims, and the Applicants respectfully request that the Examiner withdraw this rejection.

CONCLUSION

On the basis of the foregoing amendments, Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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